

A4curt

R3, R4, R5 and R6 are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; and

R7 is a hydrogen atom or an acyl group,

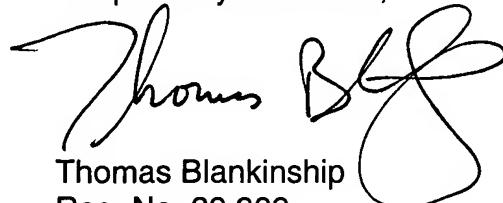
with the proviso that at least one of R1 and R2 is other than H.

REMARKS

Claims 1 to 17 are pending in this application. Claims 5, 10, 12, and 15 have been amended hereby. A marked-up version of the amended claims is attached hereto.

Applicant respectfully requests favorable consideration and that the claims of this application be passed to allowance.

Respectfully submitted,

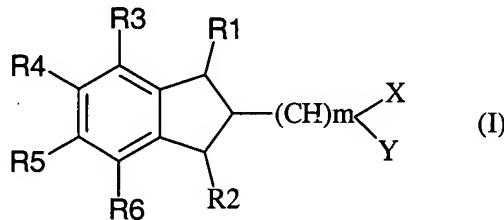


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MARKED-UP VERSION OF AMENDED CLAIMS

5. (Amended) A process for the preparation of a compound of Formula I:



[, according to claim 1,] or a pharmaceutically acceptable metabolically-labile ester or amide thereof, or a pharmaceutically acceptable salts or hydrates thereof, wherein:

R1, and R2 are selected from the group comprising:

(i) H

(ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol, -(CH₂)_n-carboxy, -(CH₂)_n-phosphono, -(CH₂)_n-phosphino, -(CH₂)_n-sulfono, -(CH₂)_n-sulfino, -(CH₂)_n-borono, -(CH₂)_n-tetrazol, or -(CH₂)_n-isoxazol, where n = 1, 2, 3, 4, 5, or 6;

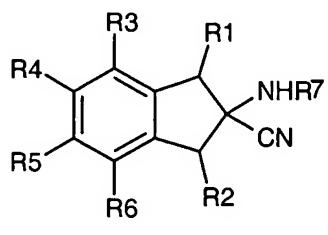
X is an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol or isoxazol;

Y is a basic group selected from the group comprising 1° amino, 2° amino, 3° amino, quaternary ammonium salts, aliphatic 1° amino, aliphatic 2° amino, aliphatic 3° amino, aliphatic quaternary ammonium salts, aromatic 1° amino, aromatic 2° amino, aromatic 3° amino, aromatic quaternary ammonium salts, imidazol, guanidino, boronoamino, allyl, urea or thiourea;

m is 0, 1;

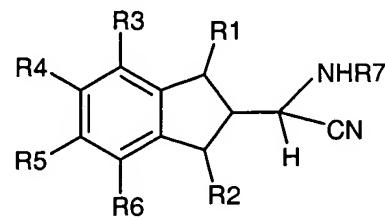
R3, R4, R5, R6 are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or an acceptable ester thereof; with the proviso that when X is COOH and Y is NH₂, then at least one of R1 and R2 is other than H, which comprises:

a) hydrolyzing a compound of formula (IIa) or (IIb):



(IIa)

or



(IIb)

wherein: R1, and R2 are selected from the group comprising:

- (i) H
- (iii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol, -(CH₂)_n-carboxy,

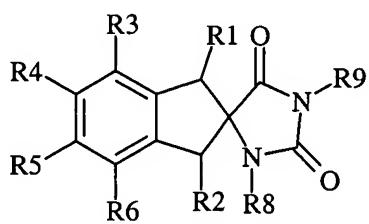
$-(CH_2)_n$ -phosphono, $-(CH_2)_n$ -phosphino, $-(CH_2)_n$ -sulfono, $-(CH_2)_n$ -sulfino,
 $-(CH_2)_n$ -borono, $-(CH_2)_n$ -tetrazol, or $-(CH_2)_n$ -isoxazol, where $n = 1, 2, 3, 4, 5$, or
6;

with the proviso that at least one of R_1 and R_2 is other than H;

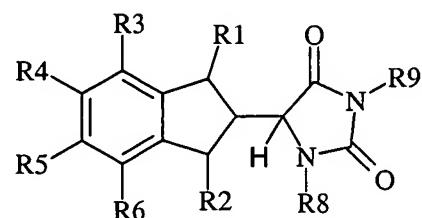
R_3, R_4, R_5, R_6 are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or an acceptable ester thereof;

R_7 is a hydrogen atom or an acyl group[. Preferred functional groups for R_7 are hydrogen and (C_2-C_6) alkanoyl group]; or

b) hydrolyzing a compound of formula (IIIa) or (IIIb):



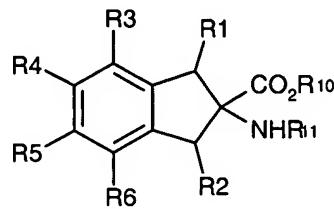
or



wherein: R_1, R_2, R_3, R_4, R_5 and R_6 are as defined above, R_8 and R_9 are each independently represent a hydrogen atom, a (C_2-C_6) alkanoyl group, a (C_1-C_4) alkyl group, a (C_3-C_4) alkenyl group or a phenyl (C_1-C_4) alkyl group wherein the phenyl is

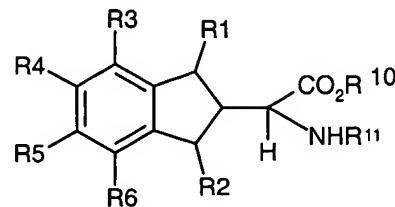
unsubstituted or substituted by halogen, (C₁-C₄) alkyl or (C₁-C₄) alkoxy, or a salt thereof, or

c) deprotecting a compound of formula (IVa) or (IV b):



(IVa)

or



(IVb)

wherein: R1, R2, R3, R4, R5 and R6 are as defined above and R10 is a hydrogen atom or a carboxyl protecting group, or a salt thereof, and R11 represents a hydrogen atom or a nitrogen protecting group;

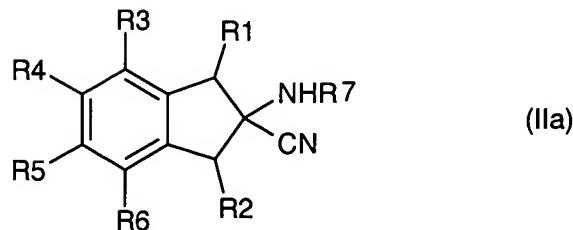
whereafter, if necessary and/or desired, the following steps are carried out:

- (i) resolving the compound of Formula I;
- (ii) converting the compound of Formula I into a non-toxic metabolically labile ester or amide thereof and/or;
- (iii) converting the compound of Formula I or a non-toxic metabolically labile ester or amide thereof into a pharmaceutically acceptable salt thereof.

9. (Amended) The use of the compound of structural formula (I) according to claim 1, in treating a neurological disease or disorder selected from the group comprising: cerebral deficits subsequent to cardiac bypass surgery and grafting, cerebral ischemia, stroke cardiac arrest, spinal cord trauma, head trauma, perinatal hypoxia, hypoglycemic neuronal damage, Alzheimer's disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, ocular damage, retinopathy, cognitive disorders, idiopathic and drug-induced Parkinson's disease, muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, drug tolerance, withdrawal, and cessation [(i.e., opiates, benzodiazepines, nicotine, cocaine, or ethanol)], smoking cessation, anxiety and related disorders [(e.g., panic attack)], emesis, brain edema, chronic pain, sleep disorders, Tourette's syndrome, attention deficit disorder, and tardive dyskinesia, wherein said use comprises administering an effective amount of a compound of formula (I)

10. (Amended) The use of the compound of structural formula (I) according to claim 1, in treating a psychiatric disease or disorder selected from the group comprising: schizophrenia, anxiety and related disorders [(e.g., panic attack)], depression, bipolar disorders, psychosis, and obsessive compulsive disorders, wherein said use comprises administering an effective amount of a compound of formula (I).

12. (Amended) A compound of formula (IIa):



wherein: R1, and R2 can each separately be selected from the group consisting of:

(i) H

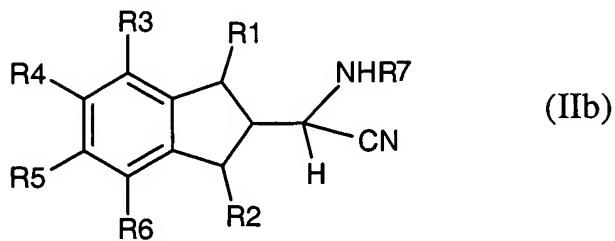
(ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol, $-(CH_2)_n$ -carboxy, $-(CH_2)_n$ -phosphono, $-(CH_2)_n$ -phosphino, $-(CH_2)_n$ -sulfono, $-(CH_2)_n$ -sulfino, $-(CH_2)_n$ -borono, $-(CH_2)_n$ -tetrazol, or $-(CH_2)_n$ -isoxazol, where $n = 1, 2, 3, 4, 5$, or 6;

R3, R4, R5 and R6 are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; and

R7 is a hydrogen atom or an acyl group[. Preferred functional groups for R7 are hydrogen and (C_2-C_6) alkanoyl groups];

with the proviso that at least one of R1 and R2 is other than H.

15. (Amended) A compound of formula (IIb):



wherein: R1, and R2 can each separately be selected from the group consisting of:

- (i) H
- (ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol, -(CH₂)_n-carboxy, -(CH₂)_n-phosphono, -(CH₂)_n-phosphino, -(CH₂)_n-sulfono, -(CH₂)_n-sulfino, -(CH₂)_n-borono, -(CH₂)_n-tetrazol, or -(CH₂)_n-isoxazol, wherein n = 1, 2, 3, 4, 5, or 6;

R3, R4, R5 and R6 are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; and

R7 is a hydrogen atom or an acyl group[. Preferred functional groups for R7 are hydrogen and (C₂-C₆) alkanoyl groups];

with the proviso that at least one of R1 and R2 is other than H.